

REMARKS

Claims 11-18 and 22 are pending.

Applicants acknowledge the Examiner's new ground of rejection of claims 11-18 and 22, under 35 U.S.C. § 112 ¶1, alleging: (A) new matter with respect to recitation in claims 11-17 and 22 of 'labeled dNTPs'; and (B) new matter with respect to recitation in claims 17 and 18 of 'bisulfite-converted sequences corresponding to SEQ ID NOS:1-12'. Applicants have amended the claims to obviate these rejections.

Applicants acknowledge the Examiner's rejection of claims 17 and 18, under 35 U.S.C. § 112 ¶2, alleging indefiniteness in view of recitation of 'bisulfite-converted sequences corresponding to SEQ ID NO:1-12.' Applicants have accordingly clarified the language of claims 17 and 18.

Applicants acknowledge the Examiner's rejections of claims 18 and 20-22, under the judicially-created doctrine of non-statutory double patenting in view of applicants' U.S. Patent No. 6,251,594, and in view of applicants' co-pending Application number 10/109,725 (now issued as U.S. 6,811,892). The present application is commonly owned with the allegedly conflicting Patents, and applicants are prepared to file a Terminal Disclaimer in compliance with 37 C.F.R. 3.73(b) upon indication of allowable subject matter.

No new matter has been added.

FORMALITIES

Applicants, in view of U.S. Patents 6,251,594 and 6,811,892, are prepared to file a Terminal Disclaimer in compliance with 37 C.F.R. 3.73(b) upon indication of allowable subject matter in the present prosecution. Applicants will also file supplementary inventor declarations upon such notice.

Rejection under 35 U.S.C. § 112 ¶1; new matter

The Examiner rejected claims 11-18 and 22, under 35 U.S.C. § 112 ¶1, as failing to comply with the written description requirement.

First, with respect to claims 11-17 and 22, the Examiner asserts that the specification as filed does not support recitation of 'labeled dNTPs' or dNTPs that are labeled with 'radiolabels or fluorescent labels and combinations thereof.' beyond ³²P-dNTPs; that is, that the applicants did not have possession of the claimed invention at the time of filing (Office Action of 20 August 2004, at page 2, paragraph 2).

Second, with respect to claims 17 and 18, the Examiner asserts that the specification as originally filed "does not provide basis for the concept of primers which are 'the bisulfite-converted sequences corresponding to SEQ ID NOS:1-12', because 'corresponding is not defined in the specification' and as such 'the claims are inclusive of primers which share any level of complementarity or identity with the sequences set forth in SEQ ID NOS:1-12' (*Id.* at page 3, under "B" and extending into page 5).

With respect to the *first* rejection in view of claims 11-17 and 22, *independent* claim 11 has been amended to clarify the claimed subject matter, in keeping with applicants' telephonic discussions with the Examiner relating to the Examiner's Proposed Examiner's Amendment of 11 May 2004 in connection with applicant's sister Application Number 10/109,725 (now issued as U.S. 6,811,892).

Specifically, claim 11 has been amended to recite "dNTPs" instead of "labeled dNTPs," and to recite "by determining the identity of the first primer-extended base" instead of "by measuring the incorporation of the labeled dNTPs," commensurate in scope with applicants' originally-filed Specification.

These amendments are fully supported by the original specification. First, as previously discussed, applicants broadly state (with reference to no specific label) (*e.g.*, at page 1, lines 10-12; as well as in the ABSTRACT at page 23) that "the inventive method provides for a bisulfite treatment of DNA, followed by methylation-sensitive single nucleotide primer extension (Ms-SNuPE), for determination of strand-specific methylation status at cytosine residues."

Second, as discussed in the interview, the specification at page 9, line 8, discloses and teaches the concept of using other labels "instead of a ³²P marker" (*e.g.*, fluorescent probes) in the

context of the present invention. Significantly, applicants teach that the essence of the present invention is to determine methylation status by determining whether (*e.g.*, for top strand analysis) the hybridized Ms-SNuPE primer is elongated (across the bisulfite-treated CpG sequence) with deoxy CTP or TTP (*see, e.g.*, Figure 2). Given this teaching, in combination with the recitation of “instead of a ³²P marker,” one of ordinary skill in the art at the time of filing would understand from the instant teachings that the dNTPs could be labeled in any way that would allow for determination of the first primer-extended base.

Thus, applicants’ conception encompasses determination of methylation state by determination of the first primer-extended base by essentially any method, and further teaches the preferred use of radiolabels or fluorescent-labels in determining the identity of the first primer-extended base.

Therefore, independent claim 11, as amended herein, is commensurate in scope with the originally filed specification.

Applicants, therefore respectfully request withdrawal of this new matter rejection with respect to independent claim 11, and thus also with respect to claims 12-17 and 22, which depend therefrom.

With respect to the *second* rejection in view of claims 17 and 18, applicants have amended the claim language in view of the Examiner’s comments to clarify the claimed invention. Specifically, claims 17 and 18 have been amended to recite “bisulfite-converted sequences of SEQ ID NOS:1-12” (emphasis added). This amendment deletes the disputed term ‘corresponding’ and clarifies, as recited in step (b) of claim 11, that the “Ms-SNuPE primer comprises from about a 15-mer to about a 22-mer length primer sequence that is complementary to the bisulfite-converted DNA sample.”

Support for this amendment, as previously discussed in the record, is found throughout the specification, for example: at the last paragraph of page 3 and first paragraph of page 4; page 4 lines 22-25; the transition paragraph between pages 7 and 8; etc. The specification teaches that bisulfite treatment converts unmethylated cytosine initially to uracil, followed by conversion to

thymidine during amplification by primer extension in the presence of dNTPs, (and this in turn reflected in the choice of nucleotides (*e.g.*, C or T) chosen in the present invention to analyze Ms-SNuPE primer extension). Additionally, for example, original claim 1 of the *parent* application (as well as the present claim 11) recites, at step (b), “reacting the genomic DNA with sodium bisulfite to convert unmethylated cytosine residues to uracil residues while leaving any 5-methylcytosine residues unchanged to create an exposed bisulfite-converted DNA sample having binding sites for *primers specific for the bisulfite-converted DNA sample*” (emphasis added).

Preferably, as taught in the Specification at page 8, lines 30-33, the Ms-SNuPE primer is designed to hybridize to a region of bisulfite-treated DNA the sequence of which is not changed by the bisulfite-treatment. However, the invention is not limited to such preferred embodiments.

Thus, the intended and supported meaning of ‘the bisulfite-converted sequences of SEQ ID NOS:1-12’ in currently amended claims 17 and 18 encompasses not only SEQ ID NOS:1-12, but also the bisulfite-treated sequences of SEQ ID NOS:1-12, as recited in the recited Markush group.

Applicants, therefore, respectfully request withdrawal of this 35 U.S.C. § 112 ¶1 rejection of claims 17 and 18 in view of applicants’ arguments and claim amendments.

Rejection under 35 U.S.C. § 112 ¶2

The Examiner rejected claims 17 and 18, under 35 U.S.C. § 112 ¶2, “as being indefinite...” (Office Action of 20 August 2004, at page 5, paragraph 3).

Specifically, the Examiner asserts that the phrase “the bisulfite-converted sequences corresponding to SEQ ID NOS:1-12” is indefinite because the term “corresponding” is not defined in the specification, as discussed above with respect to the Examiner’s paragraph one-based rejection.

As described above in detail, applicants have amended claims 17 and 18 to recite “bisulfite-converted sequences of SEQ ID NOS:1-12.”

Applicants, therefore, respectfully request withdrawal of the Examiner’s 35 U.S.C. § 112 ¶2 rejection in view of amended claims 17 and 18.

Nonstatutory Double Patenting Rejections

The Examiner has, in view of applicants' U.S. Patent No. 6,251,594 (the '594 patent) and in view of applicants' co-pending Application number 10/109,725 (now issued as U.S. 6,811,892; the '892 patent)), rejected claims 11-18 and 22, under the judicially-created doctrine of non-statutory double patenting, as claiming the same invention as that of claims 1-11 of U.S. 6,251,594, and claims 23, 24 and 29-36 of U.S. 6,811,892 (Office Action of 20 August 2004, at pages 5-8, paragraph 4). While the Examiner's present rejection with respect to application number 10/109,725 was provisional, the application has since issued.

Essentially, the Examiner asserts that some of the presently claimed subject matter, while not identical to, is nonetheless not patentably distinct from that claimed in the '594 and '892 patents.

Applicants submit that the present application is commonly owned (ASSIGNEE: University of Southern California, a not-for-profit corporation of the State of California, having administrative offices at 3716 Hope Street, Suite 313, Los Angeles, CA 90007-7377) with the allegedly conflicting '594 and '892 patents, and applicants are prepared to file a timely Terminal Disclaimer in compliance with 37 C.F.R. 3.73(b) upon the Examiner's indication of allowable subject matter.

CONCLUSION

In view of the foregoing amendments and remarks, applicants respectfully request entry of the present Response and Amendment, and allowance of all claims 11-18 and 22. No new matter has been added.

The Examiner is encouraged to phone applicants' attorney, Barry L. Davison, to resolve any outstanding issues and expedite allowance of this application.

Respectfully submitted,

Davis Wright Tremaine LLP

A handwritten signature in dark ink, appearing to read 'Barry L. Davison', written over a horizontal line.

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